Practical Guides to Cortisone Treatment

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Skin Diseases

Issued by
GLAXO LABORATORIES LTD
Makers of Cortisone Products

Cortisone and hydrocortisone have been outstandingly successful in the treatment of skin diseases, producing rapid and dramatic responses, often in conditions for which previously there was no adequate form of therapy Complete effect is usually achieved with hydrocortisone by local application, and to this method of treatment there is virtually no contra indication.

The therapeutic effects of cortisone and hydrocortisone are derived from their hormonal activity particularly in controlling abnormal changes in the collagen tissues and in suppressing inflammatory exudative, and allergic processes. Thus the substances have profound effect in the collagen diseases and in inflammatory and exudative dermatoses especially those of allergic origin.

It is essential to recognise that these ... ... purely suppressive, and that the basic cause of disease is not affected. In practice, treatment bring about complete control of ... man of the disease and, if exposure to the ... cause has been transient, a permanent effect be achieved. If the cause remains, the effect may continue only as long as treatment is progress It is a cardinal principle, therefore, ... during treatment an attempt should be made identify and eliminate the causative agent. If is not possible, some form of maintenance may be needed to ensure continued effect.

Indications TWO BROAD GROUPS

In a wide range of commonly occurring dermatoses, local treatment with hydrocortisone is fully effective and often produces a more rapid and complete effect than that attained with systemic therapy. In more severe and extensive lesions local application may be supported with systemic administration, at least until control is established. There is also a group of diseases in which the skin manifestations are only part of a general disorder and for which systemic treatment is essential. It is convenient to consider these groups separately.

GROUP ONE

Diseases Treated by Local Application

A confusing catalogue of terms has been used to describe the many dermatoses in which hydrocortisone may be employed but, broadly, they are classified by the general description dermatitis and eczema. They are too multitudinous to be discussed individually and reference can only be made to the more important groups.

CONTACT DERMATITIS including the *eczematous type of contact dermatitis, patchy eczematous dermatitis* and *chronic infectious dermatitis.*

Contact dermatitis of various forms and etiology usually

responds quite dramatically to local application of hydrocortisone, with fairly rapid relief from irritation and subsequent clearing of the physical lesions. In very severe and extensive conditions, systemic therapy may be given initially in addition. Treatment does not, of course, influence the state of sensitivity to the causative agent, which should be sought and removed. If the dermatitis was provoked by transient contact the duration of treatment can be short. But, if the excitement remains unavoidable or unidentified, treatment can be used to suppress manifestations until the cause has been removed. When sensitivity is shown to cosmetics, to furs, to fabric dyes, or to known exposure to chemicals, and also in cases of dermatitis produced by antibiotics, the causative agent is obvious and removal a relatively simple matter. In other circumstances the case may present a complex problem to be solved only by painstaking elimination of every possibility Unless this is achieved successfully relapse is likely to follow cessation of therapy

ATOPIC DERMATITIS with which may be included *infantile eczema allergic eczema food eczema exudative eczematoid dermatitis Besnier s prurigo* 'and more general terms such as *chronic eczema flexural eczema disseminated neurodermatitis*' and *eczematoid reaction of the eyes and ears*'

These are among the most commonly occurring types, especially during infancy They occur characteristical in individuals of allergic stock. The etiology is varied

often exceedingly difficult to uncover. It is understandable, therefore, that response to treatment varies. Usually it is very good, especially in infantile eczema, and is nearly always superior to that achievable with other forms of therapy Often a marked degree of improvement is achieved. Relapses are not uncommon after treatment is stopped, but response readily follows a further course of therapy

SEBORRHOIC DERMATITIS

Mild seborrhoeic dermatitis is relatively common and usually responds to ordinary measures. Some cases, however, develop extensive lesions. A chronic low-grade infection may be superimposed, particularly behind the ears, in the axilla, in the folds of the breast, and in the ano-genital region. In these cases hydrocortisone treatment will uniformly produce rapid improvement.

CHRONIC DERMATITIS OF THE HANDS AND FEET

This common disorder may produce considerable disability Care should be taken to avoid exposure to known sensitising agents, such as soaps and detergents. Hydrocortisone applied locally is usually beneficial, but the thickened skin seems to present an obstacle to successful therapy and the higher concentration may be essential to achieve effect.

LICHEN SIMPLEX CHRONICUS

This condition is marked by areas of persistent itching which provokes scratching. If inflammation and exudation

GROUP TWO

Diseases Treated by Systemic Administration

This group includes the so-called collagen diseases, *disseminated lupus erythematosus, polyarteritis, diffuse scleroderma,* and *dermatomyositis.* It also includes pemphigus, exfoliative dermatitis and drug eruptions such as urticaria and erythema multiforme.

DISSEMINATED LUPUS ERYTHEMATOSUS
POLYARTERITIS DIFFUSE SCLERODERMA
DERMATOMYOSITIS PEMPHIGUS

In these conditions adrenocortical therapy is the only effective means of control and is often life-saving. The mode of treatment is essentially similar to that used for rheumatoid arthritis although, in critical circumstances, much higher dosage may be employed. Treatment is, however, difficult. Dosage levels may need to be very high. Side-effects are a calculated risk, and a few years of relative comfort must be balanced against the otherwise inevitable progress of the condition. The degree of response attainable is largely determined by the individual circumstances.

In scleroderma and dermatomyositis the effect is dependent upon the stage to which the disease has progressed, and whether there is irreversible sclerosis and vascular obliteration.

Treatment may be started with a dosage of 100 mg daily by mouth. More may be given – sometimes very much more – if warranted by the circumstances. The manifestations are suppressed with varying rapidity usually the skin lesions clearing least quickly Within one or two weeks, when control has been established, dosage should be reduced by stages until an adequate maintenance dose has been established, usually about 25 mg. to 75 mg. daily The lower the maintenance dose the greater is the likelihood of continued therapy without side-effects.

Usually some form of maintenance therapy must be given but, in some cases of pemphigus, it seems that, following initial control, the patient may remain in remission for a considerable period without treatment. Relapse would indicate, of course, the need for resumption of therapy

During maintenance therapy exacerbations may require temporary increase in dosage; alternatively the development of hormonal side-effects, if in serious degree, may require consideration of reduction in dosage. Periods of treatment with cortisone or hydrocortisone may be interspersed with periods on corticotrophin (ACTH).

EXFOLIATIVE DERMATITIS

Response to treatment is variable, according to the cause of the condition. Cases of allergic origin apparently offer the greatest likelihood of response. Use of cortisone should

probably be tried on a tentative basis in all severe cases with extensive involvement.

DRUG ERUPTIONS such as *urticaria* and *erythema multiforme* including the *Stevens-Johnson syndrome*

These conditions frequently show rapid remission with systemic cortisone therapy. Such treatment is probably the most effective means of curtailing an attack of urticaria resulting from sensitivity to antibiotics. Good results have also been reported in *angioneurotic oedema* in which treatment may be justified if there is risk of laryngeal involvement. As these conditions are self-limiting, only a short course of treatment is required and the development of hormonal side-effects is not of practical significance.



Pharmaceutical Presentations

FOR LOCAL APPLICATION TO THE SKIN, hydrocortisone must be used, as cortisone is relatively ineffective topically. Hydrocortisone may be used as the free alcohol or as the acetate: there is no significant therapeutic difference between them and the choice rests upon pharmaceutical convenience.

FOR SYSTEMIC THERAPY either cortisone or hydrocortisone can be used. Each is equally successful therapeutically. The only significant difference in practice is that hydrocortisone is somewhat more active than cortisone, weight for weight, and is effective at about 80% of the equivalent dose of cortisone. Hydrocortisone is given by mouth. Cortisone can be injected intramuscularly but is as effective by oral administration which is, therefore, the customary method.

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Therapeutic Methods

Locally

When local treatment is to be employed, it is first necessary to select the preparation best suited for application in the particular circumstances.

The *water-miscible ointment* provides a convenient vehicle for conveying hydrocortisone to areas from which there is exudation. In other lesions the drying effect of water miscible ointment may cause some scaling and possibly soreness and, in these circumstances, the *fatty-base ointment* is preferable. Sometimes the patient may show sensitivity to one base and not the other.

The *skin lotion* is water-miscible and therefore suitable for application to weeping surfaces. Being fluid, the lotion spreads easily and can be applied to tender surfaces with minimal physical disturbance. It can be applied to a visible lesion without undesirable cosmetic effect. Hydrocortisone sometimes seems more effective in the form of the lotion than when applied in an ointment base, possibly because the lotion brings the substance into more intimate contact with the affected tissues.

The chosen preparation is usually employed in the higher concentration at first, until a response develops. It can be applied as frequently as is needed to achieve the desired effect. Usually two or three applications daily are sufficient, lengthening the interval as control is achieved. The lower concentration should then be tried and adopted if found effective. *The use of hydrocortisone is a very effective form*

of therapy but not inexpensive, so it is important to appreciate that a very thin layer of the preparation spread evenly is usually adequate. No advantage is gained by more liberal use.

Systemically

Local application of hydrocortisone is without side-effect and has been used continuously for very long periods without harm. Nevertheless, a good general principle is not to use a potent substance in excessive concentration or for an unnecessarily prolonged period. Thus, following initial therapy the interval between applications can be extended and, in self-limiting conditions, treatment can be eventually discontinued. Should the underlying cause persist or recur, the manifestations may reappear after cessation of treatment. In these circumstances a further course of treatment can be expected to be effective, or recurrence can usually be prevented by continued application every second or fourth day

When the condition is affected by concurrent infection, hydrocortisone may suppress the inflammatory changes but will have no effect on the infection itself, for which suitable antibacterial therapy should be employed.

If the lesions are particularly severe or extensive, local application of hydrocortisone may be supported by systemic therapy with cortisone or hydrocortisone for a few days until initial control is established.

For systemic therapy cortisone is usually given by mouth: alternatively hydrocortisone may be given orally or cortisone may be used by intramuscular injection. When administered intramuscularly the effect of cortisone is prolonged and one injection daily is sufficient. When either

cortisone or hydrocortisone is given by mouth the effect lasts about six hours, and four doses daily are customary

Systemic treatment normally begins with 100 mg of cortisone daily Occasionally in severe cases, 200 mg may be given daily at first and, in the collagen diseases, very much larger doses have been advocated in particular instances. If the very high dosages have been given, reduction should be effected within a few days to the customary initial level of about 100 mg, daily After a week or two, when control has been established, dosage should be reduced by stages until an adequate maintenance dosage has been determined, usually at about 25 mg to 75 mg daily The lower the dosage, the better is the prospect of continued treatment without hormonal side-effects.

Used in support of local application, systemic treatment need be continued only for the first few days.

Should systemic maintenance therapy be essential, every attempt should be made to reduce dosage by steps, continuing until treatment can be tailed off completely if possible, or replacing the dose if return of symptoms indicates need.

Hydrocortisone may be given orally at about 80% of the equivalent dose of cortisone.

Side Effects

With local hydrocortisone treatment there is virtually no contra-indication. Preparations have been applied continuously for very long periods without detectable ill-effect. Nevertheless, it is suggested that the substance should be employed in the lowest effective concentration, and attempts should be made to stop treatment, permanently or temporarily or to extend the intervals as far as possible between applications.

Theoretically use of hydrocortisone could lead to more ready spread of infection through the tissues. This is a matter for consideration in systemic treatment but, in practice, does not appear to have any practical significance in relation to local therapy Another theoretical consideration is interference with healing, but practical experience has not shown any need to regard this as being significant.

It is possible that rare individuals may show sensitivity to one base, in which case one or other of the alternative preparations should be tried.

With systemic therapy hormonal side-effects may occur if treatment is prolonged, and especially if high dosages are being used. For self-limiting diseases, a short course of treatment suffices and side-effects do not constitute a serious problem. In cases where cortisone therapy is life-saving, the occurrence of side-effects may be a calculated risk. Generally the trend of treatment is to reduce the dose level as far as possible, weighing the benefits gained against the various other hormonal effects of the corticosteroids. In most instances, adequate maintenance therapy can be

carried out with a dosage of 25 to 75 mg. of c
20 to 60 mg. of hydrocortisone) daily. Th
dosage, the greater is the likelihood of frequ
effects. With adequate supervision, early in
abnormal hormonal effects are obtained, so th
tion of the need to reduce dosage can be defi

New approach to Cortisone Manufacture

Cortisone one of the most complicated of the synthetic organic compounds yet introduced into medical practice has now been synthesised by Glaxo Laboratories in this country using a new process devised jointly with the National Institute for Medical Research This new development utilises as starting material hecogenin derived from East African sisal waste

The new method of manufacture will be put into full-scale production and then from start to finish Cortisone Glaxo will be made in the United Kingdom from materials produced in sterling areas.

In the United Kingdom and some other countries the trade names Cortelan and Ef-Cortelan are used for cortisone and hydrocortisone respectively In certain other countries however alternative names are used two of which are Cortin and Ef-Cortin

January 1956

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